Trans-1, 2-Dichloroethylene

CAS No. 156-60-5

U. S. EPA HPV Challenge Program Submission

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Submitted by

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TEST PLAN

Trans-1, 2-Dichloroethylene
CAS No. 156-60-5

HPV End Point	Information Available (Yes/No)	Acceptable (Yes/No)	Testing Required (Yes/No)
Physical-chemical Data			
Melting Point	Yes	Yes	No
Boiling Point	Yes	Yes	No
Vapor Pressure	Yes	Yes	No
Water Solubility	Yes	Yes	No
Partition Coefficient	Yes	Yes	No
Environmental Fate and Pathway			
Photodegradation	Yes	Yes	No
Stability in Water	Yes	Yes	No
Transport/distribution (Fugacity)	Yes	Yes	No
Biodegradation	Yes	Yes	No
Ecotoxicity			
Acute toxicity to fish	Yes	Yes	No
Acute toxicity to *daphnia*	Yes*	Yes	No
Acute toxicity to algae	Yes*	Yes	No
Toxicity			
Acute Toxicity	Yes	Yes	No
Repeated Dose Toxicity	Yes	Yes	No
Toxicity to Reproduction/Developmental toxicity	Yes	Yes	No
Genetic toxicity *in vitro* (Gene Mutation)	Yes	Yes	No
Genetic toxicity *in vitro* (Chromosomal Aberration)	Yes	Yes	No

*Surrogate data available on 1,1-Dichloroethylene will be used.

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1. Sponsoring Company

PPG Industries, Inc. is the manufacturer of trans-1, 2-Dichloroethylene (CAS No. 156-60-5) and is the sponsor of this substance for U.S. Environmental Protection Agency's HPV Chemical Challenge Program. The technical contact is

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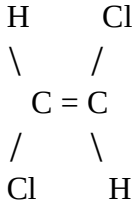
2. Test Substance

Trans-1, 2-Dichloroethylene (CAS No. 156-60-5) is a pure chemical substance. It is a clear liquid with a sweet odor. Trans-1,2-Dichloroethylene is used primarily in industry as a precision cleaning agent, a component in aerosol blends for precision cleaning, and as a source of HCl for silicon chip etching. Its molecular structure is shown below:



3. Criteria for Determining Adequacy of Data

All relevant studies were reviewed and assessed for adequacy according to the standards of Klimisch *et al*. (1977). Four reliability categories, 1-reliable without restriction, 2-reliable with restriction, 3-not reliable, and 4-not assignable, have been established and a rating of 1 and 2 were considered to be adequate.

4. Test Plan

4.1 Physical/Chemical Properties

Data are available for melting point, boiling point, density, vapor pressure, and water solubility (Encyclopedia of Chemical Technology, 1993 and Industrial Solvents Handbook, 1985). The octanol/water partition coefficient value was obtained from the Hazardous Substance Data Bank. No testing is recommended.

Melting point:	-49.4 °C
Boiling point:	48 °C @ 760 mmHg
Density:	1.45 g/cm^3 @ 20 °C
Water Solubility:	0.63 g/100 ml water @ 25 °C
Vapor pressure:	35.3 kPa @ 20 °C
Log Kow:	2.06

Several additional references for physical-chemical properties are:

Riddick J.A., *et al*., (1982). Organic Solvents: Physical Properties and Methods of Purification Techniques of Chemistry, 4th ed. New York, NY: Wiley-Interscience 2: p 1325.

US EPA: In-depth studies on Health and Environmental Impacts of Selected Water Pollutants (1978) Contract No. 68-01-4646 as cited in US EPA; Ambient Water Quality Criteria Doc: Dichloroethylenes p. B-5 (1980) EPA 440/5-80-041.

National Toxicology Program (NTP) (2002) Toxicity Studies of trans-1, 2-Dichloroethylene (CAS No. 156-60-5) administered in Microcapsules in Feed to F344/N Rats and B6C3F1 Mice. Toxicity report Series No. 55. NIH Publication No. 02-4410.

4.2 Environmental Fate/Pathways

A biodegradation study on trans-1,2-Dichloroethylene showed 93-95% total loss of the substance (of which 26-33% volatilized) after 28 days indicating moderate biodegradability (Tabak, *et al*., 1981). It is reported that hydrolysis is not expected since chlorinated ethylenes hydrolyze very slowly at environmental conditions (Hazardous Substance Data bank). Data for photodegradation and environmental transport are estimated using the EPIWIN/AOPWIN program. The estimated photodegradation hydroxyl radical rate constant is estimated to be 2.82 E-12 cm^3/molecule-sec with a half-life calculated to be 3.79 days. Level III fugacity modeling indicates that the test substance should partition to water (51.8 %), air (30.9 %), and soil (17.1 %) with smaller percentage in sediment (0.2 %). No testing is recommended.

4.3 Ecotoxicity

The effects of trans-1,2-Dichloroethylene on bluegill fish (*Lepomis macrochirus*) has been evaluated in an acute toxicity study and the 96-hour LC_{50} value under static conditions was determined to be 135,000 µg/L (US EPA, 1978). The effects of another chemical similar in structure (i.e., 1,1- Dichloroethylene) on bluegill fish were also evaluated under similar conditions and the 96-hour LC_{50} value was determined to be 73,900 µg/L. These results indicate that the toxicity of 1,1- Dichloroethylene and trans-1,2-Dichloroethylene to bluegill fish are quite similar. No other aquatic toxicity data are available for trans-1,2-Dichloroethylene. However, several other aquatic toxicity studies in various species were available for 1,1-Dichloroethylene. The LC_{50} and EC_{50} values for *Daphnia magna*, fathead minnow, and bluegill fish ranged from 11,600 to 169,000 µg/L for 1,1-Dichloroethylene. In a chronic toxicity study with fathead minnows, no adverse effects were observed at concentrations of 1,1-Dichloroethylene as high as 2800 µg/L. In a study on freshwater alga, no effects were noted at concentrations up to 798,000 µg/L of 1,1-Dichloroethylene. The LC_{50} and EC_{50} values for saltwater species including mysid shrimp, sheepshead minnow, tidewater silversides, and alga ranged from 224,000 to greater than 712,000 µg/L for 1,1-Dichloroethylene. Due to its similar structure and because the aquatic toxicity of trans-1,2-Dichloroethylene appears to be similar to 1,1-Dichloroethylene for bluegill fish, it is appropriate to use data from other aquatic toxicity studies on 1,1-Dichloroethylene as surrogate data for trans-1,2-Dichloroethylene. Thus, no further ecotoxicity testing is recommended.

4.4 Human Health Data

4.4.1 Acute Mammalian Toxicity

Trans-1, 2-Dichloroethylene showed low acute toxicity in several published data. Those studies determined to be the most robust were selected for robust summary preparation. An acute oral LD_{50} of 2122-2391 mg/kg was determined for mice (Barnes *et al*., 1985 and White *et al*., 1985) and an acute oral LD50 was determined to be 7902-9939 mg/kg for rats (Hayes *et al*., 1987). An acute inhalation LC_{50} of 24100 ppm was reported for rats (Du Pont Report 2806, 1999). Given the studies available, no testing is recommended.

Several additional references for acute toxicity data are available and are listed below:

Jenkins, L. J., Jr., *et al*. (1972). Toxicol. Appl. Pharmacol. 23, 501-510.
Freundt, K. J., *et al*. (1977). Toxicology 7, 141-153.
Munson, A. E., *et al*. (1982). Environ. Health Perspect, 43, 41-52.
Gradiski, D., *et al*. (1978). Arch. Mal. Prof., 39(4/5), 249-257.

4.4.2 Repeated Dose Mammalian Toxicity

Several subchronic studies in rodents have been conducted to evaluate the toxicity of trans-1, 2-Dichloroethylene. In an inhalation study where groups of rats were exposed whole body for 6 hours/day, 5 days/week for 90 days, the NOEL (no observed effect level) was 4000 ppm, the highest concentration tested (Du Pont Report HL-1998-00952, 1998). In a microencapsulated feeding study in rats and mice exposed for 14 weeks at concentrations of 3125, 6250, 12500, 25000 or 50000 ppm, a maximum tolerated dose was not reached and minimal toxicity was observed (NTP report, 2002). Some decreases in body weight were noted at the two highest concentrations as well as some changes in hematology parameters, liver weights, and kidney weights. However, no mortality or exposure-related changes in clinical findings, neurotoxicity endpoints, food consumption, clinical chemistry, gross lesions, or microscopic findings were noted for either sex of mice or rats. In a 90-day drinking water study, exposure of rats to 500, 1500, or 3000 mg/kg/day failed to elicit significant compound-related adverse effects on body weight, behavior, hematology, urinalysis, or serum chemistries (Hayes, J.R., *et al*., 1985). Although changes in kidney weights were noted for female rats in this drinking water study, there were no microscopic lesions noted in any organ for either male or female rats. In another drinking water study, groups of mice were exposed to trans-1, 2-Dichloroethylene up to 2 mg/ml (1/5 the LD_{50}) for 90 days and standard toxicological assessments were made (i.e., water consumption, body and organ weights, hematology and clinical chemistry, and macroscopic evaluation of organs). The only effects noted were decreased glutathione levels in males and decreased aniline hydroxylase activity in females. Additionally, various immunologic endpoints were evaluated in this study and no changes were noted in the cell-mediated immune status of either male or female mice or in the humoral immune status of females. Suppression in the humoral immune status of the male mice was observed. (Barnes, *et al.*, 1985; White, *et al*., 1985; and Shopp, *et al*., 1985). Due to number of repeated exposure studies that have been conducted and the relatively low toxicity observed, no additional testing is recommended.

One additional reference for repeated dose toxicity data that was not chosen for preparing a robust summary, is available and is listed below:

Freundt, K. J., *et al*. (1977). Toxicology 7, 141-153.

4.4.3 Genetic Toxicity

4.4.3.1. ***In vitro***

Trans-1,2-Dichloroethylene has been tested for mutagenicity in S. *typhimurium* strains TA98, TA100, TA1535, and TA1537 in the absence and presence of a metabolic activation system and produced negative results (Mortelmans *et.al*., 1986). In addition, trans-1, 2-Dichloroethylene produced no significant increase in sister chromatid exchange or chromosomal aberrations in Chinese hamster ovary (CHO) cells with or without metabolic activation (NTP report, 2002). No testing is recommended.

4.4.3.1. ***In vivo***

Trans-1,2-Dichloroethylene administered by i.p. injection at doses up to 2000 mg/kg did not induce sister chromatid exchange or chromosomal aberrations in bone marrow cells of male mice (NTP Report, 2002). In addition, trans-1,2-Dichloroethylene administered in microcapsules in feed for 14 weeks did not increase the frequency of micronucleated normochromatic erythrocytes (NCEs) in the peripheral blood of male and female mice (NTP report, 2002). No testing is recommended.

Several additional references for genetic toxicity data that were not chosen for preparing a robust summary, are available and are listed below:

Bronzetti, G., *et al*. (1984). Teratog Carcinog Mutagen 4, 365-375.
Cantelli-forti, G., *et al*. (1988). Ann N.Y. Acad. Sci. 534, 679-693.
Cerna M., *et al*. (1977). Mutation Research 46, 214-215.
Sawada, M., *et al*. (1987). Mutation Research 187, 157-163.
Tice, R.R., *et al*. (1987). Environmental Mutagenesis 9, 235-250.
Galli, A., *et al*. (1982). Soc. Ital. Biol. Sper. 58 (13), 860-863.
Simmon, V. F., *et al*. (1977). Dev. Toxicol. Environ. Sci. 2, 249-258.
Costa, A.K., *et al*. (1984) Carcinogenesis 5 (12), 1629-1936.
Tafazoli, M., *et al*. (1996) Mutation Research 371, 185-202.

4.4.4 Reproductive/Developmental Toxicity

Data from a developmental toxicity in the rats showed that trans-1,2-Dichloroethylene is not a developmental toxicant. The NOEL was less than 2000 ppm for the dam and was determined to be 6000 ppm for the conceptus (Hurtt *et al.*, 1993). In a repeated exposure study, no effects on reproductive organs, sperm motility, and vaginal cytology parameters of rats or mice were noted when the animals were fed diets containing up to 50000 ppm microencapsulated test substance for 14 weeks (NTP report, 2002). No testing is recommended.

5. Summary

Adequate data are presented to satisfy all physical/chemical properties, ecotoxicity, environmental fate, and human health data. It is concluded that no additional testing is necessary to fulfill HPV testing requirements.

6. References

(1) Kirk-Othmer, Encyclopedia of Chemical Technology, 4th ed. Volume 1: NY, NY. John Wiley and Sons, 1991-Present., V6, p 37.

(2) Flick, E.W. Industrial Solvents Handbook. 3rd ed. Park Ridge, NJ: Noyes Publications, 1985. p. 116.

(3) Tabak H., *et al*., (1981) Biodegradability Studies with Organic Priority Pollutant Compounds, Journal WPCF, 53 (10), 1503-17.

(4) US EPA: In-depth studies on Health and Environmental Impacts of Selected Water Pollutants (1978) Contract No. 68-01-4646 as cited in US EPA; Ambient Water Quality Criteria Doc: Dichloroethylenes p. B-5 (1980) EPA 440/5-80-041.

(5) Barnes, D.W., V.M. Sanders, K.L. White, Jr., G.M. Shopp, Jr., and A.E. Munson, (1985) Toxicology of Trans-1,2-Dichloroethylene in the Mouse, Drug Chem. Toxicol., 8(5), 373-392.

(6) White, K.L. Jr., D. W. Barnes, V.M. Sanders, G.M. Shopp, Jr., and A.E. Munson, (1985) Immunotoxicological Investigations in the mouse: General Approach and Methods, Drug Chem. Toxicol., 8(5), 299-331.

(7) Hayes, J.R. *et al*. (1987). Journal of the American College of Toxicology, 6(4), 471-478.

(8) E.I. du Pont de Nemours and Company Report DuPont-2806, Dated 12-29-99

(9) E.I. du Pont de Nemours and Company, Report HL-1998-00952, Dated 12-1-98.

(10) National Toxicology Program (NTP) (2002) Toxicity Studies of trans-1,2-Dichloroethylene (CAS No. 156-60-5) Administered in Microcapsules in Feed to F344/N Rats and B6C3F1 Mice. Toxicity Report Series No. 55. NIH Publication No. 02-4410.

(11) Shopp, G.M. Jr., D.W. Barnes, V.M. Sanders, K.L. White, Jr., and A.E. Munson, (1985) Humoral and Cell-mediated Immune Status of Mice Exposed to Trans-1,2-Dichloroethylene, Drug Chem. Toxicol., 8(5), 393-407.

(12) Mortelmans, K., S. Haworth, T. Lawlor, W. Speck, B. Tainer, and E. Zeiger, (1986) Salmonella Mutagenicity Tests: II. Results from the Testing of 270 Chemicals. Environ. Mutagen. 8(Suppl. 7), 1-119.

(13) Hurtt, M.E., R. Valentine, and L. Alvarez, (1993) Fundamental and Applied Toxicology 20, 225-230.